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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,807	02/27/2004	Benjamin Tjon	NWB1135118	5631
26389 7590 04/10/2012 CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC 1420 FIFTH AVENUE SUITE 2800 SEATTLE, WA 98101-2347				
EXAMINER				
JUEDES, AMYE				
ART UNIT		PAPER NUMBER		
1644				
NOTIFICATION DATE		DELIVERY MODE		
04/10/2012		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efiling@cojk.com

Office Action Summary**Application No.**

10/789,807

Applicant(s)

TJOA ET AL.

Examiner

AMY JUEDES

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2012.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1 and 4-29 is/are pending in the application.
- 5a) Of the above claim(s) 4-7, 10-12, 16, and 24-29 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1, 8, 9, 13-15 and 17-23 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-326)
Paper No(s)/Mail Date ____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 2/13/12 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/13/12 has been entered.

Claims 4 and 8 have been amended.

Claims 1 and 4-29 are pending.

Claims 4-7, 10-12, 16, and 24-29 stand withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 1, 8-9, 13-15, and 17-23 are under examination.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-9, 13-15, and 17-23 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient guidance to differentiate immature dendritic cells having CD1a and decreased expression of CD14, from non-activated monocytic precursors, as broadly claimed.

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the

invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The 'amount of guidance or direction' refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims are drawn to a method of differentiating monocytic precursors into immature dendritic cells having decreased expression of CD14 and increased expression of CD1a comprising contacting non-activated monocytic precursors with GM-CSF in the absence of additional cytokines. The state of the art is such that obtaining immature dendritic cells with GM-CSF in the absence of additional cytokines is extremely unpredictable. For example, Chaperot et al. teach a method identical to that of the instant claims, including culturing the monocytic precursors in non-adherent bags, but fail to obtain CD1a+ immature dendritic cells after culture in GM-CSF in the absence of additional cytokines. Chaperot et al. teach isolating the monocytic precursors by various methods including cytophoresis, density gradient preparation, and negative selection (see page 1668, in particular), which are conditions disclosed by the instant specification as "non-activating". Likewise, Bernard et al., 1998 (of record) teach a method identical to that of the instant claims, including culturing in PFTE bags, but again fail to obtain immature dendritic cells with reduced CD14 expression by culture with GM-CSF in the absence of additional cytokines. Furthermore, Sallusto et al. (of record) culture monocytic precursors in the presence of a medium containing 10% serum along with GM-CSF alone, which as disclosed by the instant specification prevents tight adherence and activation of the cells. However, Sallusto et al. fail to obtain CD1a+ immature dendritic cells. While other references (i.e. Matera et al. and Kasinrerker al.) do obtain a population of CD1a+ cells displaying decreased expression of CD14 by culture in GM-CSF in the absence of additional cytokines, it is not readily apparent which factors are critical for successfully obtaining said cells compared to the methods of Sallusto et al, Bernard et al., or Chaperot et al. Thus, based on the extremely unpredictable nature of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims.

The instant specification teaches that the critical factor in obtaining immature dendritic cells by culture with GM-CSF in the absence of additionally cytokines relates to the activation status of the monocytic precursors. The specification teaches that the monocytic precursors should be isolated and cultured in such a way as to prevent their activation. For example, the instant specification discloses that non-activated precursors can be obtained by inhibiting the tight adhesion of monocytic precursors to the culture surface. The specification discloses on page 6 that this can be accomplished by a using low avidity culture vessels, or by including a high concentration of animal serum in the culture. The instant specification further discloses various methods for isolating the monocytic precursors such that they are non-activated, but the disclosed methods are the same as those taught in the prior art, including aphaeresis, centrifugation, or positive/negative selection. The instant specification further provides specific examples in which monocytic precursors are cultured with GM-CSF in the absence of additional cytokines to obtain

CD1a+ immature dendritic cells. The examples disclose culturing the cells in low-avidity bags, or with a high concentration of serum protein. However, both Bernard et al. and Chaperot et al. have performed the method using a low avidity culture vessel and isolation of the cells using a non-activating method, and failed to obtain CD1a+ immature dendritic cells with reduced CD14 expression. Moreover, Sallusto et al. have cultured monocytic precursors with 10% serum, which according to the instant specification, should prevent tight adherence (and hence activation) of the precursors. However, Sallusto et al. also failed to obtain immature dendritic cells after culture in GM-CSF alone. Thus, it must be assumed that other critical factors are required to successfully perform the method of the instant claims, either in the cell isolation protocol or the cell culture conditions. Therefore, based on the unpredictability of the art, the instant specification does not provide sufficient guidance to enable one of skill in the art to obtain "non-activated" precursor as broadly claimed, that would result in a CD1a+ immature dendritic cell after culture with GM-CSF in the absence of additional cytokines.

Applicant's arguments filed 2/13/12 have been fully considered, but they are not persuasive.

Applicant argues that none of the cited references teach the same method as recited in the instant claims, and that there is no evidence that the monocytes do not interact with the "non-adherent bag" to induce macrophage differentiation. Applicant notes that the skilled artisan would be able to alter the methods of Bernard et al. and Chaperot et al. using the teachings of the instant specification to obtain immature dendritic cells. Applicant argues that the specification teaches the use of Teflon bags and discloses that a high concentration (e.g. about 1% to about 10%) of animal or human protein can be used to further decrease adhesion. Applicant notes that Chaperot et al. and Bernard et al. teach using 2% or 5% plasma or serum, which comprises only 7% protein. Applicant argues that this is below the concentration of human or animal protein defined in the present specification as being desired to inhibit macrophage formation.

The instant claims are not limited to a method of culturing cells with a particular concentration of human or animal protein. The instant claims are directed to a method wherein adhesion is prevented through the use of a PTFE low avidity vessel, exactly as taught by Bernard et al. and Chaperot et al. Claim 13 even specifies that the culture medium is serum free (i.e. encompassing a method performed in the absence of serum proteins). All of the examples provided by the instant specification employ a culture medium comprising 2% human serum albumin. Thus, it is clear that the inclusion of

human serum albumin is a critical element of the claimed method. A claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling. In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The specification does not enable the method as broadly claimed, wherein adhesion of the precursors is prevented by any means, including culture in a PTFE low avidity vessel, since the art teaches that culture in such a low avidity culture vessel is not effective for generation of immature dendritic cells having no expression of CD14, as claimed.

3. No claim is allowed.

4. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY JUEDES whose telephone number is (571)272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Kolker can be reached on 571-272-3181. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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